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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,595	06/07/2002	Albrecht E. Sippel	WEICKM 14	5887

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MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

EXAMINER

GAMETT, DANIEL C

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/869,595	Applicant(s) SIPPEL ET AL.	
	Examiner Daniel C. Gamett	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 March 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4, 8, 10-72 and 74-78 is/are pending in the application.
- 4a) Of the above claim(s) 11-13, 29, 38, 44-60, 64-66, 71 and 74-78 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 8, 10, 14-28, 30-37, 39-43, 61-63, 67-70, 72, 79 and 80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
6) <input type="checkbox"/> Other: _____ |
|--|---|

DETAILED ACTION

1. A summary of the telephone interview of March 16, 2005 is included on form PTO-413.
2. The amendments of 03/17/2005 have been entered in full. Claims 5-7, 9, and 73 are cancelled.

New claims 79 and 80 have been added. This application contains claims 44-60, 64-66, 71, and 74-78, drawn to an invention nonelected with traverse in the Response filed on 11/01/2004.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.
3. Claims 1-4, 8, 10, 14-28, 30-37, 39-43, 61-63, 67-70, 72, 79, and 80 are under examination.

Response to Arguments

Re Objections to the Disclosure

4. Applicant's argument that there is no statutory requirement that the specification follow the preferred layout outlined in MPEP601 is noted; however Applicant is nevertheless encouraged to follow the guideless for drafting a nonprovisional patent application un 35 U.S.C. 11(a) set for therein.

Claim Rejections withdrawn.

35 USC § 112, second paragraph

5. Amendments to claims 10, 22, 30, 33, and 42 have obviated the rejection concerning ranges in section 7 (p. 5) of the prior Office Action, and so this rejection is hereby withdrawn. The rejection of claim 5 is rendered moot by the cancellation of claim 5.
6. The amendment to claim 23 obviates the rejection for lack of antecedent basis in section 8 of the prior Office Action, and so said rejection is hereby withdrawn.

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7. The rejection of claim 73 in section 10 of the prior Office Action is rendered moot by the cancellation of claim 73.

Claim Rejections maintained

35 USC § 112, second paragraph

8. The amendments to claim 1 are not sufficient to overcome the grounds of rejection of claims 1-4, 8, 10, 14-28, 30-35 made in section 6 (p.4) of the Office Action mailed on 12/17/2004. The amended claim recites *an* amino acid sequence for each of three domains, but does not specify which amino acids are required, included, or excluded. Therefore the claim remains vague.
9. The rejection of claims 36,37, 39-43, 61-63, 67-70, and 72 set forth in section 6 (p.4) of the prior Office Action for recitation of “nuclear receptor” is maintained. Although claim 1 has been amended to recite “steroid receptor”, claims 36 and 39 (and claims dependent therefrom) still recite “nuclear receptor”, which introduces vagueness as to the nature of the second domain for reasons of record.
10. The rejection of claim 72 set forth in section 9 (p.6) of the prior Office Action is maintained.

Applicant's amendment is not sufficient to overcome the lack of clarity in claim 72 for the following reasons. For convenience, the amended claim is presented here:

A method for identifying a ligand for a binding section of a steroid receptor, a compound able to alter the binding activity of a ligand-binding section of a steroid receptor in relation to a ligand, or a polypeptide or protein having a ligand-binding function of a steroid receptor, where a presumed ligand, a presumed modifying compound or a polypeptide or protein with presumed ligand-binding function, which have been obtained by derivatizing one or more times a ligand, modifying compound, polypeptide or protein identified by means of the assay as claimed in claim 36.

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The phrase beginning with “where a presumed ligand...” appears to be attempting to introduce limitations, but it does not make sense. Elimination of the word “which” would at least make grammatical sense. If the recited “polypeptide or protein identified by means of the assay as claimed in claim 36” is meant to be a species of the “polypeptide or protein having a ligand-binding function of a steroid receptor” recited earlier in claim 72, then this recitation lacks antecedent basis because claim 36 is drawn to an assay for “determining the suitability of a test substance as ligand for a receptor section of a nuclear receptor” and so would not identify a protein with ligand binding function.

35 USC § 112, first paragraph, Written description

11. Rejection of claims 1-4, 8, 10, 14-28, 30-37, 39-43, 61-63, 67-70, 72, 79, and 80 as failing to comply with the written description requirement, set forth in section 12, (pp.7-9) of the prior office action is maintained. Applicant's arguments filed 03/17/2005 have been fully considered but they are not persuasive. Applicant argues that a patent need not teach, and preferably omits, what is well known in the art. While amino acid sequences for farnesylation and prenylation signals, steroid receptors, and Ras proteins maybe taught in the art, the sequences may not be identical from reference to reference. As noted in the prior Office Action, references for the source materials for the working example are not provided in the disclosure. Applicant further argues that sequences are not required because the novelty of the sequence is not at issue in the present case. While the components of the fusion protein of the amended claims are largely known, when building the fusion protein of the invention, the arrangement of the components is critical. The sequences of the domains may be individually obtainable, but it is far from obvious how one should put them together to make a functional

molecule. Furthermore, even with the added limitations, claim 1 still defines a large, undescribed genus of proteins. The second domain may be derived from receptors for any of estrogen, progesterone, androgens, glucocorticoids, mineralocorticoids, or Vitamin D3. Binding of ligand is claimed to either positively or negative regulate the Ras protein in the third domain. This broad genus is not adequately represented by the single disclosed species. Finally, claims 36 and 39 still recite “nuclear receptor” and so the argument concerning the breadth of this term, presented on p. 8 of the prior Office Action, still applies to these claims and their dependents. New claims 79 and 80 fail to overcome the lack of written description in the base claims and so are included in this maintained rejection.

35 USC § 112, first paragraph, Enablement

12. Rejection of claims 1-4, 8, 10, 14-28, 30-37, 39-43, 61-63, 67-70, 72, 79, and 80 as failing to comply with the enablement requirement, set forth in sections 14-19, (pp.10-15) of the prior office action is maintained. Applicant's arguments filed 03/17/2005 have been fully considered but they are not persuasive. Applicant argues that the test of enablement is not whether any experimentation would be required, but whether, if experimentation is necessary, it is undue and that the amendments have attempted to make the set of possible combinations finite and manageable by placing structural limitations on the domains of the fusion proteins. However, the changes do not overcome the enablement issues originally raised and introduce new issues. For example, in section 17 of the prior Office Action, it was noted that the specification provided no example or guidance regarding the alternative function of the third domain “when there is binding of a ligand to the second domain the third domain cannot exert activity”. As previously noted, this claimed mode of action is only

a theoretical possibility; nobody knows if it can actually be done. The only working example in the specification works in exactly the opposite manner. Therefore, achieving this functionality would require considerable experimentation even when the choices for the first and second domains are limited. Secondly, the amended claims do not specify that the Ras amino acid sequence of the third domain is bereft of its lipid modification signal, the CAAX box. Therefore the claims indicate a protein that could be anchored to the inner surface of the plasma membrane at both ends. If functional at all, the Ras signaling activity of such a protein would almost certainly not be regulated as desired by ligand binding in the second domain. Furthermore, although the amendments create an impression of introducing limitations, in fact they do not. In Claim 1 as currently drawn, each domain comprises *an* amino acid sequence with a specified functionality. This open language permits, for example, the third domain to comprise as little as two consecutive amino acids from a naturally occurring Ras protein, as long as the domain is able to activate a signaling pathway connected to Ras. Finally, claims 36 and 39 still recite “nuclear receptor” and so the enablement issues that stem from the breadth of this term, presented on pp. 12-13 of the prior Office Action, still applies to these claims and claims dependent therefrom. New claims 79 and 80 fail to overcome the lack of enablement in the base claims and so are included in this maintained rejection.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1, 14, 21, and 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15. In Claim 1 as currently drawn, each domain comprises *an* amino acid sequence with a specified functionality. This open language permits, for example, the third domain to comprise as little as two consecutive amino acids from a naturally occurring Ras protein, as long as the domain is able to activate a signaling pathway connected to Ras. Therefore the metes and bounds of the claim cannot be determined.

16. Claim 14 recites the limitation " the third domain comprises *an* amino acid sequence which is derived from the amino acid sequence of a naturally occurring Ras protein..." in "a fusion protein as claimed in claim 1". The nature of the lack of clarity in this claim is dependent upon the construction of claim 1, which as stated above is unclear. If claim 1 is limited to naturally occurring Ras sequences, then there is insufficient antecedent basis for artificial derivatives of Ras proteins. With artificial derivatives precluded, only natural variants remain, and claim 14 fails to further limit claim 1, which already recites naturally occurring proteins. Furthermore, claim 14 places no limit on the extent of Ras protein sequences that must be retained; it could be as little as two consecutive amino acids. Therefore the metes and bounds of the claim cannot be determined.

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17. Claim 21 recites a “cell as claimed in claim 19, characterized in that it comprises two or more said fusion proteins.” Does this mean proteins expressed by two or more different constructs or does it simply indicate that at least two molecules of protein are expressed in the cell?
18. Claim 26 recites the limitation “activatability of the signal pathway connected to a Ras protein is temperature-dependent in the absence of fusion protein” in a cell as claimed in claim 23. There is insufficient antecedent basis for this limitation. In the cell of claim 23, the intrinsic pathway connected to a Ras protein is inactivated; it has no “activatability” and therefore cannot be temperature-dependent, which means it is active at a permissive temperature. Claims 27-31 are rejected as being dependent on indefinite base claim 26.

Conclusion

19. No claims are allowed.
20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
9 June 2005


BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600